

## **DETAILED ACTION**

### ***Status of the Claims***

Claims 1-3, 6-10, 14-19, and 25-28 are pending and under examination.

Amendments to claims 1 and 15 are acknowledged.

Claims 4-5, 11-13 and 20-24 have been canceled.

### ***Continued Examination Under 37 CFR 1.114***

A request for continued examination under 37 CFR 1.114, including the fee set forth in 37 CFR 1.17(e), was filed in this application after final rejection. Since this application is eligible for continued examination under 37 CFR 1.114, and the fee set forth in 37 CFR 1.17(e) has been timely paid, the finality of the previous Office action has been withdrawn pursuant to 37 CFR 1.114. Applicant's submission filed on 18 November 2010 has been entered.

### ***Withdrawn Rejections***

Rejection of claims 1-3, 6-10, 14-19, and 25-28 under 35 U.S.C. 112, second paragraph, are hereby rejected in view of Applicant's arguments and amendments.

### ***Claim Objections***

Claim 14 is objected to because of the following informalities: claim 14 depends from claim 12, which was canceled as per Applicant's response on 15 March 2010. Prior to its cancelation claim 12 depended from claim 11 (similarly canceled), which

depended from claim 1. *See* Claims filed on 12 August 2009. For the sake of current prosecution claim 14 will be examined as depending from claim 1. Appropriate correction is required.

### ***Claim Rejections - 35 USC § 103***

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negated by the manner in which the invention was made.

The factual inquiries set forth in *Graham v. John Deere Co.*, 383 U.S. 1, 148 USPQ 459 (1966), that are applied for establishing a background for determining obviousness under 35 U.S.C. 103(a) are summarized as follows:

1. Determining the scope and contents of the prior art.
2. Ascertaining the differences between the prior art and the claims at issue.
3. Resolving the level of ordinary skill in the pertinent art.
4. Considering objective evidence present in the application indicating obviousness or nonobviousness.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was

not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

Claims 1, 8-10, 15-19, 27, and 28 are rejected under 35 U.S.C. 103(a) as being unpatentable over U.S. Pat. No. 5,866,321 to **Matsue *et al.*** ("Matsue") in view of U.S. Pat. No. 5,922,537 to **Ewart *et al.*** ("Ewart"). Both Matsue and Ewart are already of record.

Matsue describes a biosensor with a reactant immobilized on a first electrode. *See* column 9, line 56 to column 10, line 17; Figure 1A and 1B. The reactant may be a substance that binds directly to the analyte, but which themselves will not undergo any chemical changes, as exemplified by an antibody against an antigen analyte. *See* column 5, lines 10-20. The reactant is also exposed to a second electrode such that the reactant is between the first and second electrodes. *See* column 9, line 56 to column 10, line 17; Figure 1A and 1B. Matsue also describes using the biosensor to detect the presence of an analyte that binds to the reactant, such that binding between the reactant and analyte causes an electrical signal that can be detected. *See* column 7, lines 34-37; column 9, lines 30-42. With this description, Matsue teaches the instant claims except for a ferroelectric transducer.

Ewart describes a method of optimizing a capacitive sensor device by including a dielectric made from ferroelectric ceramic in a biosensor device, such as barium titanate. *See* column 14, lines 10-38. The dielectric material comprises a planar layer

on top of electrodes, which may facilitate linking of recognition molecules (i.e. probe molecules) or other bioactive molecules to the surface. See column 14, line 60 to column 15, line 3. An advantage of the dielectric layers on the electrode is that these layers have the ability to amplify or attenuate the sensitivity of the device. See column 15, lines 3-13.

With the foregoing description in mind, one of ordinary skill in the art would have found it obvious to modify Matsue's method by incorporating Ewart's barium titanate as a ferroelectric layer. The combination would therefore produce a sensor by which the reactants are immobilized on the planar ferroelectric layer. The skilled artisan would have been motivated to make the modification because Ewart indicates that this type of arrangement would optimize capacitance sensing by amplifying the sensitivity of the device. The skilled artisan would have recognized that capacitance sensing would apply to Matsue's method since Matsue's biosensor can detect any type of electrical measurement, and capacitance sensing is one type of electrical measurement. Since Matsue's biosensor fits this description, the skilled artisan would have found it obvious to apply Ewart's barium titanate ferroelectric layer to Matsue's biosensor. Furthermore, since Ewart describes the ferroelectric layer as applicable in a biosensor the skilled artisan would have had a reasonable expectation of success.

Regarding claims 8 and 17, Ewart teaches that the ferroelectric material can be a ferroelectric polymer. See column 15, lines 50-51.

Regarding claims 9 and 18, Ewart describes the ferroelectric layer is a thin film. See Figure 8.

Regarding claims 10 and 19, Matsue teaches that the analyte can be either an antigen or antibody. *See* column 14, lines 24-30.

Regarding claim 16, since the electrodes have stored charge for performing capacitive detection, a voltage source is necessarily provided.

Regarding claims 27 and 28, Matsue and Ewart (together "Matsue") do not teach a thin film that is "about 180 nm thick." However, the skilled artisan would have found it obvious to arrive at this dimension based on the doctrine of routine optimization. In a case decided by the precursor to the Federal Circuit, the Court stated that a claim is not allowable where the skilled artisan could have arrived at the claim through routine experimentation on the optimum or workable ranges of the claim. *In re Aller*, 220 F.2d 454, 456 (CCPA 1955) (stating "where the general conditions of a claim are disclosed in the prior art, it is not inventive to discover the optimum or workable ranges by routine experimentation.") In *Aller*, the claims were directed to a process taught by the prior art, except for a specific temperature and acid concentration range. *Id.* The Court, however, held that the claims were not patentable since the skilled artisan could have arrived at the claimed ranges through routine optimization. Similar to the *Aller* case, Matsue teaches all the limitations of claims 27 and 28, except for a size. However, Ewart suggests that a capacitive sensor can be optimized. *See* column 14, lines 10-11. Accordingly, the skilled artisan would have recognized that Matsue's general conditions could be used as a basis for performing routine experimentation to arrive at an optimal thickness for the transducer thin film, especially since Ewart indicates that such experimentation is applicable to the thin film.

Claims 2, 3, 6, and 7 are rejected under 35 U.S.C. 103(a) as being unpatentable over **Matsue** in view of **Ewart**, as applied to claim 1 above, and further in view of U.S. Pat. No. 7,163,659 to **Stasiak et al.** ("Stasiak"). Stasiak is already of record.

Matsue in view of Ewart (together "Matsue") disclose a method for detecting a biological analyte within a sample and a device for use with said method, wherein the device comprises two electrodes, wherein on of the electrodes has disposed thereon a ferroelectric transducer coated with probe, as detailed above.

However, Matsue in view of Ewart fail to disclose the various signal and electric response schemes particular to dependent claims 2, 3, 6, and 7.

Stasiak teaches that capacitance detection is useful for obtaining both qualitative and quantitative information. See column 12, lines 54-68. Stasiak teaches this type of measurement in the context of a sensor comprising two electrodes, one with a functional layer thereon and the other in contact with a sample such that the sample is between the two electrodes. See column 6, lines 52-65; column 12, lines 1-22; and Figure 7. The electrode with the functional layer comprises a dielectric material, see column 3, lines 27-29 and column 4, lines 9-12, and can have immobilized biomolecules, such as antibodies, thereon, see column 8, lines 23-26. Moreover, Stasiak indicates that dual-electrode biosensors with reactants in between can be used for capacitance sensing.

Regarding claims 2 and 3, Stasiak teaches performing parallel tests, one test being a control. See column 12, lines 14-22. With this method, a comparison of

electrical signals can be performed and the quantity of analyte can be determined. *Id.* It would have been obvious to modify Matsue's method to incorporate Stasiak's comparison test, since doing so would reveal a more accurate determination of analyte quantity. Moreover, regarding claim 3, implicit in this description is the correlation between signal level and analyte concentration.

Regarding claims 6 and 7, Stasiak teaches the step of applying an electrical current to at least one of the electrodes. *See* column 6, lines 65-66. As would have been apparent to one of ordinary skill in the art, capacitive sensing necessarily involves either applying a current and measuring a change in voltage or applying a voltage and measuring a change in current. Accordingly, it would have been obvious to perform either method using Matsue's method.

Claim 14 is rejected under 35 U.S.C. 103(a) as being unpatentable over **Matsue** in view of **Ewart** as applied to claim 1, and further in view of U.S. Pat. No. 4,810,639 to **Pankratz** (already of record).

Matsue and Ewart (together "Matsue"), described above, do not teach the step of "removing a remaining portion of said sample," as claimed.

Pankratz teaches a washing step to remove sample constituents and contaminants not bound to the solid phase. *See* column 8, lines 41-45.

With the foregoing description in mind, one of ordinary skill in the art would have found it obvious to modify Matsue's method by including a washing step to remove unbound analytes, as taught by Pankratz. The skilled artisan would have been

motivated to perform the modification based on Pankratz's teaching that the washing step removes contaminants. Indeed, this step would prevent any interference by the contaminants in affecting the assay result. Moreover, Pankratz's washing step is provided in the form of an immunoassay, which is within the scope of Matsue's assay. Accordingly, the skilled artisan would have had a reasonable expectation of success in combining Pankratz's step with Matsue's method.

Claims 25 and 26 are rejected under 35 U.S.C. 103(a) as being unpatentable over **Matsue** in view of **Ewart** as applied to claims 1 and 15 above, and further in view of U.S. Pat. No. 7,527,720 to **Ishimaru et al.** ("Ishimaru") (already of record).

Matsue and Ewart (together "Matsue") do not teach a movable electrode.

Ishimaru states that where a biosensor is sandwiched by a pair of electrodes, one of the electrodes can be movable in a manner facing the other electrode. See column 4, lines 31-39.

With the foregoing description in mind, one of ordinary skill in the art would have found it obvious to modify Matsue's method to include a movable electrode. The movable electrode would be the electrode not attached to the reactant. The skilled artisan would have made the modification because Ishimaru indicates that this technique is well known in the art. Moreover, this would allow the skilled artisan to obtain an optimal signal since the movable electrode could be adjusted appropriately. For the same reason, the skilled artisan would have had a reasonable expectation of success.

***Response to Arguments***

Applicant's arguments filed 18 November 2010 have been fully considered but they are not persuasive.

**PIECEMEAL ANALYSIS**

In response to applicant's arguments against the references individually, one cannot show nonobviousness by attacking references individually where the rejections are based on combinations of references. See *In re Keller*, 642 F.2d 413, 208 USPQ 871 (CCPA 1981); *In re Merck & Co.*, 800 F.2d 1091, 231 USPQ 375 (Fed. Cir. 1986).

*i. Matsue reference.*

Applicant argues that the Matsue reference does not teach "immobilizing said analyte in said sample on a ferroelectric transducer" or even the use of ferroelectric materials as substrate for the sample, but rather teaches away from the invention by teaching use of a non-ferroelectric substrate. See Applicant's Arguments, page 8, second and third paragraphs. These arguments are not found persuasive.

As noted in the 35 U.S.C. 103(a) rejection of claim 1 above, Matsue is not being relied upon for teaching a ferroelectric material, but rather Ewart is relied upon for teaching this limitation. Moreover, Applicant's interpretation of Matsue as teaching away from the invention by teaching use of a non-ferroelectric substrate, is flawed. The teaching upon which is Applicant's argument relies upon is actually drawn to a substrate 1 upon which an electrode 2 is disposed that has the reactant 3 coated thereon. See

Matsue, column 9, lines 57-63; Figures 1A and 1B. On the contrary, the instant claim is drawn to an electrode upon which a transducer is disposed that has probe molecules coated thereon. Therefore, it is clear that the substrate disclosed by Matsue is not structurally or functionally related to any of the features recited in the instant claim.

*ii. Ewart reference.*

Applicant argues that Ewart does not teach "a ferroelectric transducer having a planar test surface comprising a coating of probe molecules". This is not found persuasive.

As detailed in the 35 U.S.C. 103(a) rejection of claim 1 above, Ewart does in fact teach a ferroelectric transducer having a planar test surface comprising a coating of probe molecules". (The following text is copied from the 103(a) rejection above). Ewart describes a method of optimizing a capacitive sensor device by including a dielectric made from ferroelectric ceramic in a biosensor device, such as barium titanate. See column 14, lines 10-38. The dielectric material comprises a planar layer on top of electrodes, which may facilitate linking of recognition molecules (i.e. probe molecules) or other bioactive molecules to the surface. See column 14, line 60 to column 15, line 3.

Applicant also argues that Ewart does not teach "establishing an electric field to polarize said analyte in said sample, or sensing an electric response of said ferroelectric transducer resulting from the effect of said electric field in said sample on said ferroelectric transducer, and indicative of the presence of said analyte in said sample."

However, this is not found persuasive as it is the Matsue reference being relied upon for teaching all of the limitations of claim 1 except for the ferroelectric transducer.

Applicant further states that Ewart teaches away from the invention in that "by removal of such analyte particles from the test surface, the capacitance of the device has changed and hence, a measure of the amount of analyte in the sample can be detected by use for example, of the biosensors of FIGS. 10 and II." This is also not found persuasive.

Ewart is relied upon for its teaching that a ferroelectric material would generally benefit capacitance measurements. Such measurements occur whether an analyte is added or removed from an electrode surface. Indeed, both scenarios would cause a change in capacitance, and it is specifically the "change" in capacitance that is measured. *See* Ewart, column 14, lines 10-20. Accordingly, Ewart is applicable to Matsue. Furthermore, Ewart states that the disclosed biosensor test surface can be used in a variety of assay techniques and is designed to determine analyte concentration by virtue of addition or displacement of the labeling entities to or from the test surface. *See* Ewart, SCOPE OF THE INVENTION, column 1, Lines 5-28. Thus Ewart suggests detection of analyte by immobilization on probe molecules.

*iii. Stasiak reference.*

Applicant's argument that Stasiak does not teach limitations of independent claim 1 are not found persuasive. As explained *supra*, Matsue in view of Ewart teach all of the limitations of instant claim 1. Stasiak is not relied upon for teaching any of the limitations of instant claim 1.

NO TEACHING, SUGGESTION, OR MOTIVATION TO COMBINE

In response to applicant's argument that there is no teaching, suggestion, or motivation to combine the references, the examiner recognizes that obviousness may be established by combining or modifying the teachings of the prior art to produce the claimed invention where there is some teaching, suggestion, or motivation to do so found either in the references themselves or in the knowledge generally available to one of ordinary skill in the art. See *In re Fine*, 837 F.2d 1071, 5 USPQ2d 1596 (Fed. Cir. 1988), *In re Jones*, 958 F.2d 347, 21 USPQ2d 1941 (Fed. Cir. 1992), and *KSR International Co. v. Teleflex, Inc.*, 550 U.S. 398, 82 USPQ2d 1385 (2007). In this case, Ewart provides the motivation for combining a ferroelectric transducer with the method and device of Matsue by pointing out that an advantage of a dielectric layer (i.e. ferroelectric transducer) is their ability to amplify or attenuate the sensitivity of a biosensor device. See Ewart, column 14, lines 20-38 and column 15, lines 7-13.

### ***Conclusion***

No claims are allowed.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Erik B. Crawford whose telephone number is (571)270-1011. The examiner can normally be reached on Monday through Friday, 8:00am to 5:00pm..

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Mark Shibuya can be reached on (571)272-0806. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see <http://pair-direct.uspto.gov>. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

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